PXE Awareness

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

Volume 14, Issue 2, July 2008

Salt Lake City, here we come!!!

Holiday Inn Hotel & Suites welcomes NAPE

Conference October 4-5

Mormon Temple

Temple Square

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

8760 Manchester Road, St. Louis, MO 63144-2724
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NAPE, a non-profit 501(c)(3) support group whose mission is to provide education and support for PXE-affected persons, publishes *PXE Awareness*. Articles in this newsletter are provided for information only and are not a substitute for professional medical advice. You should not use information in this newsletter to diagnose or treat medical or health conditions. Please consult your healthcare provider before beginning or changing any course of treatment.

Board of Directors

Board of Medical Advisors

Table of Contents

President's Message

Dear NAPE Friends,

It is with sadness that I report the death of Dr. Robert Hoehn of Denver. Dr. Hoehn, plastic surgeon, developed procedures to safely eliminate PXE skin folds. The procedure demonstrated that PXE skin folds can be successfully treated. Dr. Hoehn's wife, Nancy, shared with me her husband's pride in his work with PXE patients and with NAPE. He was very pleased to serve as a NAPE Medical Advisor. PXE patient lives were enhanced through his knowledge, skill and compassion. Please join me in remembering Dr. Hoehn's contributions. Our thoughts and prayers are with Nancy and the family in their loss.

Genentech's Avastin/Lucentis story was covered widely in the news media. We include in this issue a brief update, including the NIH study to compare the relative effectiveness of the two drugs.

Our annual meeting will be held in Salt Lake City, October 4 and 5. Several changes in our format will be initiated in response to member suggestions. Saturday's program will begin with a poster session, followed by an informal researcher round table. Participating physicians and researchers will interact with each other about PXE research directions and respond to audience questions.

Saturday will be a full day with lunch, breaks and dinner provided so that we can fit in as many informative sessions as possible. Sunday will be an important day, but will not consume the entire day. Please see the enclosed schedule. PXE finally is getting considerable research attention. There will be much to learn and to talk about. Please sign up as soon as possible so that we in the NAPE office can work with our hotel to assure a successful conference.

Dr. Kattesh Katti's research which NAPE is funding builds on previous research by his lab at the University of Missouri, Columbia. Initial results are quite promising and you can read about them in this issue. As well, please find Dr. Berthold Struk's presentation on PXE inheritance and the difficult choices often faced by PXE patients. "Recent Research Studies" feature four studies which explore PXE as a metabolic disorder. "Vision Regeneration Research" announces significant and hopeful discoveries for those of us who have suffered retina damage.

Finally, please know that we are most grateful to those who have responded to last issue's call for donations. We hope that others who are helped by NAPE's services will contribute so that we can continue our work.

Sincerely,

Fran Benham

The Genentech Saga

By Fran Benham

Genentech's decision to continue to make Avastin available for vision loss care has been well covered by local and national news services. We are grateful for our physicians who made the case for us, and we thank Genentech for a most helpful decision.

Genentech has launched a major campaign to make its own case for Lucentis for vision loss treatment. Meetings which feature an ophthalmologist and an AMD patient provide excellent information about central vision loss resulting from AMD. They provide information about the success of Lucentis and they do not mention Avastin. When questioned about Avastin, they respond with data about Lucentis. They make clear that no patient should fail to receive treatment because of financial problems.

Genentech provides an assistance program for those who cannot afford Lucentis. No such program is available for Avastin for vision loss care. Lucentis is administered monthly for $2,000 per injection. Avastin can be given monthly or less frequently

according to need at a cost of $50 per injection. Genentech's website, www.gene.com, provides details for the Lucentis assistance program. Your ophthalmologist will need to participate in your application and can help you in the process.

The National Institutes of Health is funding a clinical trial comparison of the two Genentech drugs. Lucentis was presented for and gained Food and Drug Administration approval for the treatment of wet macular degeneration. Avastin was earlier approved for cancer treatment, but was not presented for approval for vision loss care. With FDA approval, Lucentis is covered by Medicare at a cost of $24,000 per year. The typical treatment term is two years. Some 200,000 older adults are diagnosed with AMD each year. Given the cost to our government, the decision was made for a government-funded comparison study. NAPE will follow this study and keep our readers informed.

6 Pseudoxanthoma Elasticum: Inheritance, Difficult Choices and Cardiovascular Manifestations

by B. Struk, MD, PhD
Franz-Volhard-Clinic and
Max-Delbrueck-Center Berlin Buch

PXE No Choice

- PXE patients
  - Can‘t choose their parents, nobody can
  - Therefore, can't influence their genetic make-up

PXE Disease Definition

- PXE is a heritable systemic (metabolic?) disorder affecting the elastic tissue, characterized by systemic manifestations,

typically first in skin, then in the eyes and cardiovascular system
    - accelerated aging of the organ systems involved

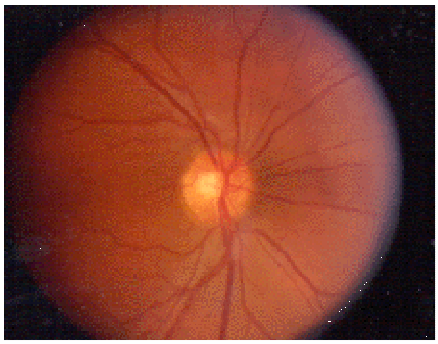
PXE Epidemiology

- Prevalence approximately 1 in 50,000 to 1 in 100,000
- Mean age of onset 13 years (range 2-40 yrs)
- No racial predilection
- 2 to 1 female preponderance
- Previously under-diagnosed
- Now over-diagnosed ??

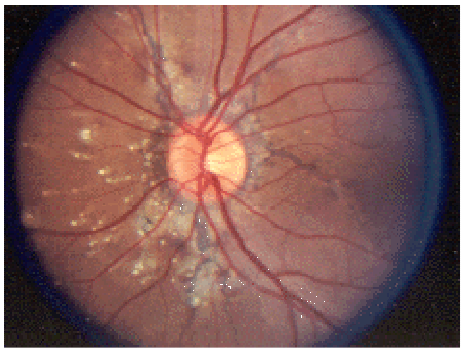
PXE Clinical Manifestation Sites

- Skin
- Eyes
- Cardiovascular System

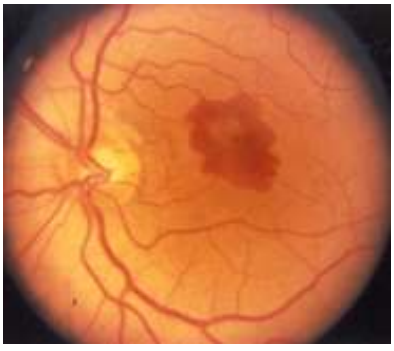
PXE Retinopathy Characteristics



Normal fundus



PXE fundus with
- angioid streaks,
- atypical drusen

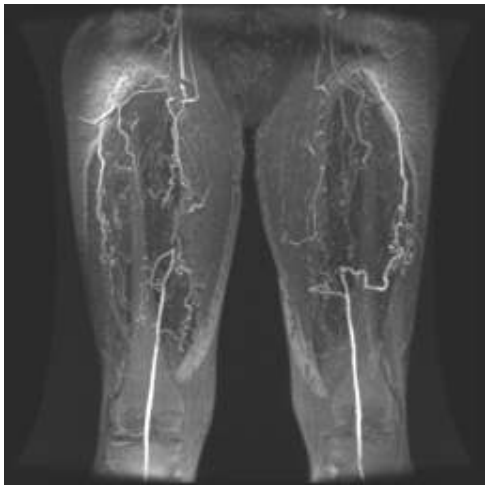


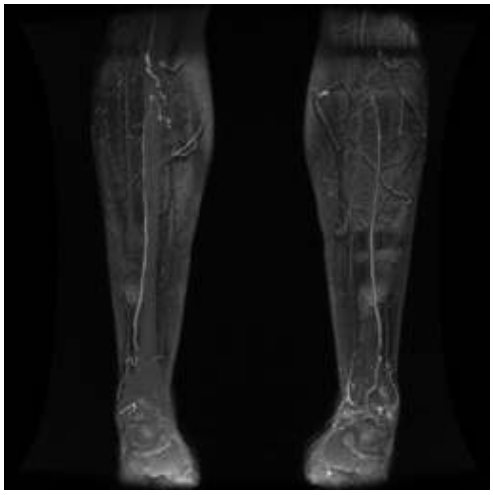
PXE fundus with
- angioid streaks,
- retinal hemorrhage

PXE Cardiovascular System

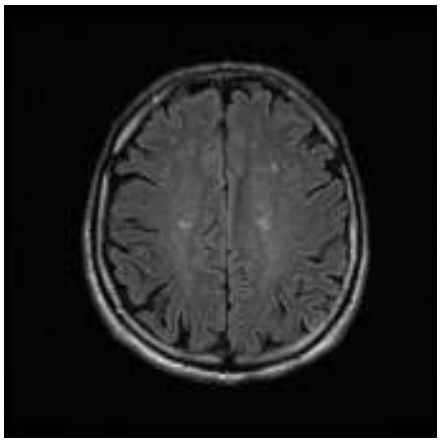
- Heart
  - Coronary artery disease
  - Endocardial thickening
    - Mitral valve prolapse

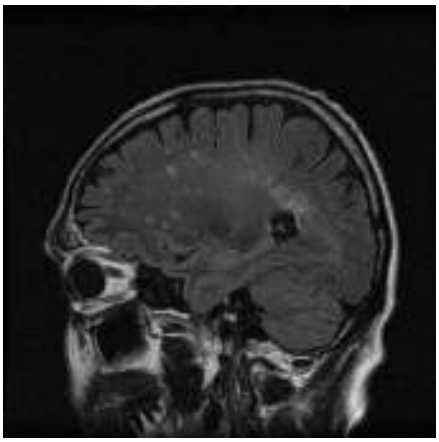
- Peripheral Artery Disease
  - Carotid arteries
  - Gastrointestinal arteries
  - Arteries of upper and lower extremities





- Small Vessel Disease
  - Brain → Mental fatigue syndrome
  - Gut
  - Kidney





PXE Cardiovascular Phenotype

- Intermittent claudication 20-30%
- Hypertension, angina pectoris, heart attacks, stroke 20%
- Gastrointestinal hemorrhage 5-13%
    - Intermittent claudication and angina pectoris in PXE become prevalent 10 to 20 years earlier than in the general population

PXE Pathology

- Calcification (mineralization) of elastic fibers
- Increase of elastic fibers in elastic tissue (dermis)
- Increase in glycosaminoglycans in elastic tissue (dermis) (glucoseamine, hyaluronic acid, chondroitin sulfate B)

PXE Cardiovascular Pathophysiological Mechanism

- "vascular stiffening"

PXE Diagnostic Classification Prior to "Molecular Diagnosis"

Category I (3 major criteria)	Category IIa (1 major criterion and 2 minor criteria)	Category IIb (1 major and 1 minor criterion)	Category IIc (1 major and 1 minor criterion)	Category IId (2 minor criteria)
1. characteristic flexural skin lesions	1. angioid streaks	1. angioid streaks	1. angioid streaks	1. family history of PXE in first-degree relatives
2. elastic fiber calcification-lesional skin	2. elastic fiber calcification-nonlesional skin	2. elastic fiber calcification-nonlesional skin	2. family history of PXE in first-degree relatives	2. elastic fiber calcification-nonlesional skin
3. ocular disease in adults	3. family history of PXE in first-degree relatives			

PXE Angioid Streaks

Disorders other than PXE in which angioid streaks have been observed:

- Paget's Disease (Osteitis Deformans)
- Marfan's Syndrome
- Ehlers-Danlos Syndrome
- Beta Thalassemia
- Sickle cell hemoglobinopathies
- Hereditary spherocytosis
- Idiopathic thrombocytopenic purpura
- Tumoral calcinosis
- Lead poisoning
- Cowden's Syndrome
- Pituitary tumors
- Acromegaly
- Familial polyposis
- Nevus of Ota (oculodermal melanocytosis)

PXE Mutation Analysis

- Mutation screening in 89 PXE affected individuals
  - representing 170 distinct PXE chromosomes
  - belonging to 81 families
    - 61 families (75%) with PXE in a sibpair of 1 generation (recessive mode of inheritance)
    - 11 families (13.5%) with PXE in 1 person of single generation (sporadic mode of inheritance)
    - 9 families (11%) with PXE either in first degree cousins, or two or three family generations (possible dominant mode of inheritance)

PXE Mutation Detection Rate

- Potentially disease causing mutations were found in 165 of 170 chromosomes
- Mutation detection rate of 97%

PXE Mutation spectrum in ABCC6

- 5 distinct large deletions
- 32 missense mutations
- 8 nonsense mutations
- 1 small insertion
- 7 small deletions
- 6 splice site mutations

PXE Molecular Genetics

- Interestingly, the frequent PXE mutations originate from founder alleles

PXE From Bench to Bedside

- Genotype phenotype analysis in the current set of families reveals:
    - All affecteds according to category I diagnostic criteria always carry two mutation alleles (*homozygotes, compound heterozygotes*)
    - All affecteds according to category II diagnostic criteria always carry one mutation allele (heterozygotes)

- Homozygotes and compound heterozygotes show the full expression of the disease according to category I diagnostic criteria:
    - Characteristic flexural skin lesions
    - Elastic fiber calcification of lesional skin
    - Ocular disease in adults (retinal hemorrhages with subsequent central visual field loss)

- Heterozygotes can show the expression of a *forme fruste* of PXE that is characterized by category II diagnostic criteria, but not by long-term complications of the disease:
  - Angioid streaks
  - Elastic fiber calcification of non-lesional skin
  - Family history of PXE in first degree relatives
  - No retinal bleeding and no central visual field loss

- Therefore, PXE (full phenotype expression with long term complications) is solely recessively inherited.
- This has profound consequences for the correct genetic counseling of families with PXE
- Mutations cause loss of protein function.

PXE From Bench to Bedside – Conclusions

- Familial PXE mutation analysis in *ABCC6*
  - Enhances and refines the clinical diagnostic criteria of the disease
  - Demonstrates a recessive-only mode of inheritance of the full phenotype
  - Allows for the molecular exact discrimination of full phenotype expression against the *forme fruste*
  - And therefore, allows early individual risk prediction with regard to potential long-term disabling disease complications

- Pfendner EG, et al.
  - J Med Genet. 2007 Jul 6; [Epub ahead of print] PMID: 17617515 [PubMed - as suplied by publisher]
  - *"An interesting observation was the absence of macroscopic skin lesions in 4 patients, although skin biopsy revealed typical histological characteristics of PXE*
  - *One patient had significant ophthalmologic complications, suggesting that this individual was not a carrier*
  - *In three of these patients, a complete genotype was found, confirming the clinical diagnosis and emphasizing that skin features, although present in the*

majority of PXE patients, <u>are not always mandatory for the diagnosis</u>

- Why did Pfendner et al. find this, but not us?
  - Selection bias
    - Their patients were referred through ophthalmologists
    - Our patients had to pass the dermatologist first
  - Potentially wrong clinical assessment
    - Missed subtle skin lesions, potentially false positive mutation analysis
    - PCR contamination
    - Sample mix-up

- Is the result by Pfendner et al valid?
- Yes, it is an important observation, but
  - Further independent observation is needed
  - If it exists it is very rare
  - It is something to keep in mind,
    but will not change the principal approach towards diagnosing PXE in the first place

PXE From Bench to Bedside – Conclusions in Short

- Molecular analysis confirms in PXE:
  - The skin might not tell it all
  - Molecular diagnosis is needed for the unambiguous diagnosis and for the safest risk prediction

Choices for Patients With PXE

- Seek molecular diagnosis
  - if clinical criteria don‘t fit and PXE is still suspected
- No disease inheritance to the next generation through a single parent

- If you suffer from PXE
  - Adjust your life style to minimize your CV risk factors
  - Get monitored for cardiovascular disease manifestations of PXE

PXE Personal Cardiovascular Risk Control

- Keep normal body weight
- No BMI > 26 for male and > 25 for female
- Do regular exercise
- Eat healthy

Suggested Reading:
Eat More, Weigh Less by Dean Ornish, MD
Dr. Dean Ornish's Program for Reversing Heart Disease by Dean Ornish, MD

PXE Professional Medical
Cardiovascular Risk Management I:

- Annual lipid profile:
  - Cholesterol (HDL, LDL, VLDL, Chylomicrons)
  - Triglycerid
  - Lipoprotein a [Lp (a)]
  - C-reactive Protein
  - (Homocystein) no longer recommended

PXE Professional Medical
Cardiovascular Risk Management II:

- Annual echocardiography and stress test
- Two annual 24-hour blood pressure monitorings
- Exclusion of diabetes mellitus as additional risk factor

PXE Professional Medical
Cardiovascular Risk Management III:

- No causal treatment available
- Treatment of hyperlipidemia
  - LDL < 100 mg/dl (statins)
- Treatment of high blood pressure
- Treatment of coronary artery disease
- Treatment of peripheral artery disease

“Green” Gold Nanoparticles

The work of Dr. Kattesh V. Katti and his colleagues at the University of Missouri-Columbia has evolved over the recent past to develop non-toxic delivery of drugs to treat leaky vasculature in cancer and in such vision disorders as AMD and PXE. Gold nanoparticles were effectively coated with gum arabic, used widely in human food preparation. Recently, the more ubiquitous cheaper plant extract, soy, was found also to provide for effective delivery of drugs in animal experiments. Soy coated gold nanoparticles produced unexpected efficacy in reducing retinal bleeding in rats. Further study will follow in animal models more similar in physiology to humans.

NAPE is supporting this study in part to include PXE. The broader study focuses on AMD as well as PXE. It is hoped that a new method of treatment using significantly less medication with less potential for side effects will be developed.

Dr. Katti’s work has been widely reported in the scientific press worldwide. Following are some of those sources.

“Nanotherapy for AMD,” *Ophthalmology Times Europe*. May 21, 2008. http://www.oteurope.com/ophthalmologytimeseurope/

“Plant extracts as nontoxic nanoparticle coating for nanomedicine applications,” by Michael Berger, *Nanowerk LLC*, February 12, 2007. http://www.nanowerk.com

Accepted for publication: “Soybeans as a Phytochemical Reservoir for the Production and Stabilization of Biocompatible Gold Nanoparticles,” by Kattesh V. Katti, et al, in *Small Nano Micro* (manuscript #200800525, Wiley-VCH)

Recent Research Studies

Editor's Note: The following abstracts are of interest to those who try to stay current with PXE research. The first study from the Netherlands Cancer Institute in Amsterdam has attracted attention by NAPE members. It describes early efforts to understand PXE as a metabolic disorder. This is sure to be a topic of interest at our conference in October.

Does the absence of ABCC6 (Multidrug Resistance Protein 6) in patients with pseudoxanthoma elasticum prevent the liver from providing sufficient vitamin K to the periphery?

Borst P., **van de Wetering K.**, **Schlingemann R**.

The Netherlands Cancer Institute, Division of Molecular Biology, Amsterdam, The Netherlands.

Pseudoxanthoma elasticum (PXE) is an autosomal recessive disease characterized by a progressive mineralization of connective tissue, resulting in skin, arterial and eye disease. Classical PXE is caused by mutations in the ABCC6 gene, which encodes a member of the ABCC (MRP) family of organic anion transporters. Recent studies on Abcc6(-/-) mice show that the absence of ABCC6 in the liver is crucial for PXE and confirm the "metabolic disease hypothesis" for PXE, which states that tissue calcification is due to the absence of a plasma factor secreted from the basolateral hepatocyte membrane. We propose that this plasma factor is vitamin K (precursor). We propose that vitamin K (precursor) is secreted by ABCC6 from the liver as a glutathione -(or glucuronide)-conjugate and that this supplements the vitamin K need of peripheral tissues that receive insufficient vitamin from the diet, because dietary vitamin K is effectively extracted from blood by the liver. Peripheral tissue vitamin K is needed for the gamma-carboxylation of glutamate residues in proteins known to be required for counteracting calcification of connective tissue throughout the body. Our hypothesis explains the known facts of PXE and also explains why PXE-like symptoms can occur in patients with mutations in the gamma-glutamyl carboxylase gene (encoding the enzyme responsible for protein carboxylase) and in

rats treated with vitamin K antagonists. The hypothesis implies that the symptoms of PXE can be prevented or mitigated by providing patients (intravenously) with a form of plasma vitamin K (precursor) that can be used by peripheral tissues.

(http://www.ncbi.nlm.nih.gov/pubmed/18469514)

Pseudoxanthoma elasticum: reduced gamma-glutamyl carboxylation of matrix gla protein in a mouse model (Abcc6-/-).

Li Q., **Jiang Q.**, **Schurgers L.J.**, **Uitto J**.

Department of Dermatology and Cutaneous Biology, Jefferson Medical College, Philadelphia, PA 19107, USA.

Pseudoxanthoma elasticum (PXE), a heritable multi-system disorder manifesting with ectopic mineralization of soft connective tissues, is caused by mutations in the ABCC6/MRP6 gene/protein system, but the mechanisms how the ABCC6 mutations lead to aberrant mineralization are currently unknown. In this study, we utilized a transgenic mouse model, Abcc6-/-, to examine the mineralization processes. We focused on matrix gla protein (MGP) which has been shown to be critical, when activated by gamma-carboxylation of glutamyl residues, for prevention of unwanted mineralization. The concentration of MGP in the serum of Abcc6-/- mice was significantly reduced when compared to wild-type controls ($p<0.004$). More importantly, MGP isolated from the liver of Abcc6-/- mice was largely under-carboxylated and therefore possesses no activity. Finally, examination of the Abcc6-/- mice revealed association of total and under-carboxylated forms of MGP with ectopic mineralization while the gamma-carboxylated form was essentially absent. These results suggest that MGP in Abcc6-/- mice is largely in inactive form and is unable to prevent the unwanted mineralization of connective tissues in PXE.

(http://www.ncbi.nlm.nih.gov/pubmed/17942075)

The local calcification inhibitor matrix Gla protein in pseudoxanthoma elasticum.

Hendig D., **Zarbock R.**, **Szliska C.**, **Kleesiek K.**, **Götting C**.

Institut für Laboratoriums- und Transfusionsmedizin, Herz- und Diabeteszentrum Nordrhein-Westfalen, Universitätsklinik der Ruhr-Universität Bochum, Bad Oeynhausen, Germany.

OBJECTIVES: Recent studies have revealed the involvement of calcification inhibitory proteins in the pathogenesis of pseudoxanthoma elasticum (PXE). DESIGN AND METHODS: We analyzed serum concentrations of the calcification inhibitor matrix Gla protein (MGP) in a large cohort of patients suffering from PXE (n=101), 34 first-degree relatives and 67 healthy controls. Moreover, we determined the distribution of the two MGP promoter polymorphisms c.-7G>A and c.-138T>C in the three cohorts. RESULTS: We found significantly lower total MGP concentrations in the sera of PXE patients compared to healthy controls (p=0.0002). Furthermore, higher serum MGP concentrations could be correlated with a later PXE onset. Analysis of MGP promoter polymorphism frequencies revealed one MGP haplotype to be a potential protective co-factor in PXE. CONCLUSIONS: Our findings point to a role of the local calcification inhibitor MGP in PXE manifestation.

(http://www.ncbi.nlm.nih.gov/pubmed/18222176)

18

Matrix Gla protein is involved in elastic fiber calcification in the dermis of pseudoxanthoma elasticum patients.

Gheduzzi D., **Boraldi F.**, **Annovi G.**, **DeVincenzi C.P.**, **Schurgers L.J.**, **Vermeer C.**, **Quaglino D.**, **Ronchetti I.P**.

Department of Biomedical Sciences, University of Modena and Reggio Emilia, Modena, Italy.

Mature MGP (Matrix gamma-carboxyglutamic acid protein) is known to inhibit soft connective tissues calcification. We investigated its possible involvement in pseudoxanthoma elasticum (PXE), a genetic disorder whose clinical manifestations are due to mineralization of elastic fibers. PXE patients have

lower serum concentration of total MGP compared to controls (P<0.001). Antibodies specific for the noncarboxylated (Glu-MGP) and for the gamma-carboxylated (Gla-MGP) forms of MGP were assayed on ultrathin sections of dermis from controls and PXE patients. Normal elastic fibers in controls and patients were slightly positive for both forms of MGP, whereas Gla-MGP was more abundant within control's than within patient's elastic fibers (P<0.001). In patients' calcified elastic fibers, Glu-MGP intensively colocalized with mineral precipitates, whereas Gla-MGP precisely localized at the mineralization front. Data suggest that MGP is present within elastic fibers and is associated with calcification of dermal elastic fibers in PXE. To investigate whether local cells produce MGP, dermal fibroblasts were cultured in vitro and MGP was assayed at mRNA and protein levels. In spite of very similar MGP mRNA expression, cells from PXE patients produced 30% less of Gla-MGP compared to controls. Data were confirmed by immunocytochemistry on ultrathin sections. Normal fibroblasts in vitro were positive for both forms of MGP. PXE fibroblasts were positive for Glu-MGP and only barely positive for Gla-MGP (P<0.001). In conclusion, MGP is involved in elastic fiber calcification in PXE. The lower ratio of Gla-MGP over Glu-MGP in pathological fibroblasts compared to controls suggests these cells may play an important role in the ectopic calcification in PXE.

(http://www.ncbi.nlm.nih.gov/pubmed/17724449)

Vision Regeneration Research

20

Dr. Dong Feng Chen and her colleagues at Harvard Medical School Schepens Eye Research Institute have announced a discovery that may offer hope to those who have lost vision due to macular degeneration, retinitis pigmentosa and other disorders which harm the retina. Their discovery, published in the March issue of *Investigative Ophthalmology and Visual Science*, is an unexpected role for Müller cells which had been understood to have the role of keeping the retina clear of waste and debris. Chen's team noticed that when the chemicals glutamate and aminoadipate (a derivative of glutamate) were injected into the eye, Müller cells began to divide and change into other cell types. The Müller cells acted as "progenitor" cells, dividing and changing into limited types of cells including photoreceptor cells. The newly minted cells then migrated to sites in the retina where they were needed. Further experiments confirmed the potential of Müller cells to be used in retina repair. Chen indicates that more study will seek to determine this possibility. If it works it means that the retina can repair itself with appropriate therapy. Study will be made of the process in animal models bred to have such disorders as macular degeneration and retinitis pigmentosa. This significant research was also reported in lay language in *Science Daily* at

http://www.sciencedaily.com/releases/2008/03/080318113517.htm

Mark your calendar!

2008 NAPE Annual Conference
October 4 and 5

The conference will be held in Salt Lake City, Utah, at the Holiday Inn Hotel & Suites just west of the Salt Lake City International Airport. Free airport shuttle, free on-site parking available.

More information will be mailed separately to NAPE members who register for the conference by September 18. The conference registration form is at the end of this issue.

2008 Conference Information

When: Saturday, October 4 through Sunday afternoon, October 5. Schedule included in this issue and posted on the NAPE website. It will also be mailed to those who register by September 18.

Where: Holiday Inn Hotel & Suites – Airport West
5001 W. Wiley Post Way, Salt Lake City

Room rate (single and double) $79 if reserved by September 18, otherwise you will be charged the going rate. Call 801-741-1800 or 1-800-345-8082 and state that you are a NAPE conference registrant.

Meals: Conference registration fee of $50 per person includes Saturday lunch and dinner plus breaks. You are responsible for your own breakfast on Saturday and Sunday.

Air-travel: Holiday Inn Hotel & Suites is just west of the Salt Lake City International Airport (STC). A free shuttle is available to the hotel from the airport.

Driving directions: From I80W, take exit 114, turn left at first light (Wiley Post) to the hotel; From I80E, take exit 113/5600W, turn left onto 5600W, right to Amelia Earhart Drive, right on Charles Lindbergh Drive, left on Wiley Post to the hotel

2008 NAPE CONFERENCE SCHEDULE

Holiday Inn Hotel & Suites – Airport West
Salt Lake City, Utah

Saturday, October 4, 2008
(Breakfast on your own)

8:00-9:30am	Poster Session
9:30am	Conference Convenes. Welcome by Dr. Fran Benham
9:45-10:45am	Research Round Table – Meet our physicians and researchers for an introduction to their PXE work and informal discussion of issues with members
10:45-11:00am	Break
11:00-noon	Group Discussion on Nutrition in PXE. Discussion leader, Dr. Berthold Struk, MD, PhD
Noon-1:30pm	Buffet Lunch (included in your registration)
1:30-3:00pm	Update on Vision Research. University of Utah Moran Eye Center Faculty Member
3:00-5:30pm	Free Time
5:30-10:00pm	Dinner (included in registration) A leisurely meal with time to visit with conference peers and researchers.

2008 NAPE CONFERENCE SCHEDULE
continued

Sunday, October 5, 2008
(Breakfast on your own)

24

8:30-10:00am	PXE Inheritance, Cardiology Issues and Varied PXE Manifestations - Dr. Berthold Struk, MD, PhD
10:00-10:15am	Break
10:15-11:30am	PXE Research Project, “Green” Nanoparticles, - Dr. Kattesh Katti, PhD
11:30am-noon	Business Meeting
Noon	Adjournment

NAPxE – National Association for Pseudoxanthoma Elasticum

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Website: www.napxe.org Email: napestlouis@sbcglobal.net

REGISTRATION FORM – 2008 ANNUAL MEETING

Saturday, October 4 – Sunday, October 5, 2008

The registration fee is $50 per person and includes Saturday lunch, dinner and break and the Sunday break plus all programs

NAME _____ **PHONE** _____

ADDRESS _____ **FAX** _____

CITY _____ **EMAIL** _____

STATE _____ **ZIP** _____ **COUNTRY** _____

ARRIVAL DATE _____

NUMBER ATTENDING MEETING _____ x $50.00 = AMOUNT ENCLOSED $_____

NAME(S) OF GUEST(S) ATTENDING WITH YOU:

You are responsible for making your own hotel reservations. Please call the **Holiday Inn Hotel & Suites, Airport West in Salt Lake City, Utah, at 801-741-1800 or 1-800-345-8082**. Be sure to **call by September 18, 2008**, and say you are with NAPE to get the group rate of $79 per night (single or double) plus tax. Parking onsite is free and hotel-airport shuttle is available free.

Payment of the registration fee must accompany this form. Please make your check payable to NAPE, Inc., in U.S. currency. We cannot accept credit card payments. Mail your registration and check to NAPE at the address shown above. We will send you a confirmation packet if registration is received by September 18.

If you require special assistance to participate fully, please provide a written description of your needs on the back of this form. Vegetarian meals can be accommodated.

SIGNATURE _____ **DATE** _____

Please mail this form to NAPE with payment by September 18, 2008
CANCELLATIONS ARE NOT REFUNDABLE AFTER SEPTEMBER 18, 2008

National Association for Pseudoxanthoma Elasticum

8760 Manchester Rd., St. Louis, MO 63144-2724

Donations - Membership

No membership fee is required, although donations are needed to pay operational expenses, including telephone, fax, email, website and newsletter services.

Donations can be made in Honor or Memory of a loved one, for the Research Fund and/or for the Low-Vision Fund. All donations are tax deductible in the USA.

❒**Operations** ❒**Honor** ❒**Memory** ❒**Low-Vision** ❒**Research**

Name of Loved One: _____
Address for Acknowledgement:

PLEASE COMPLETE THE SECTION BELOW IF YOU HAVE PXE, THINK YOU HAVE PXE, OR ARE FILLING THIS OUT FOR SOMEONE ELSE

Name: _____ **Phone:** _____

Email: _____ **Fax:** _____

Address: _____

City: _____ **State:** _____ **Zip:** _____ **Country:** _____

Male ❒ **Female** ❒ **Birthdate:** _____ **Age:** _____

I am diagnosed with PXE ❒**Yes** ❒ **No** **Newsletter:** ❒ **Print** ❒ **CD**

Are you legally blind? ❒ **Yes** ❒ **No** ❒ **Email notification**

Do others in your family have PXE? ❒ **Yes** ❒ **No** **If so, who? (Mother, Father, Sibling, etc. & Name)** _____

_____

Please list any medical problem(s) you are experiencing: e.g., eye involvement, skin lesions, heart problems, gastric bleeding, etc., and comments/questions (use another page if required):

_____

_____

_____

Are you willing to be contacted by another who wishes to talk with someone else who has PXE? ❒ **Yes** ❒ **No**

PXE Pals

To help protect the privacy of our PXE Pals online, please contact the NAPE Office at 314-822-1170 to request a contact.

Have You Changed Your Address?

Please help by letting us know. Please be sure to print your new zip code number, including the extra four digits, if possible. When we use the full zip code, our costs of mailing in the United States are lower. Please help.

New Address
Name: _____

Street: _____

City, State, Zip _____

Old Address
Name, if different: _____

Street: _____

City, State, Zip _____

PLEASE PRINT NEATLY

National Association for Pseudoxanthoma Elasticum
NAPE, Inc.
8760 Manchester Road
St. Louis, MO 63144-2724

ADDRESS SERVICE REQUESTED